UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

In re Fenofibrate Patent Litigation	:	ECF Case Case No. 1:11-md-2241 (JSR) (THK)

DEFENDANTS' OPENING CLAIM CONSTRUCTION BRIEF

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Defendants submit this brief in support of their constructions of the disputed terms in U.S. Patent No. 7,101,574 B1 ("the '574 patent") and U.S. Patent No. 7,863,331 B2 ("the '331 patent") (together, "the patents-in-suit").[1] *See* Ex. 8, Docket Entry (DE) 3 (Joint Claim Construction Statement).[2]

INTRODUCTION

Lupin owns the rights to the prescription drug ANTARA®, which is used to treat patients with high cholesterol and triglycerides. According to Plaintiffs, this drug and its method of use are covered by the '574 and '331 patents. Lupin did not develop ANTARA®. Indeed, before purchasing the rights to that drug, Lupin had applied to market a *generic* version, just as the Defendants have done here. In Lupin's FDA application for its generic version of ANTARA®, Lupin certified that its generic products would not infringe the '574 patent, *and that this patent is invalid*. Ex. 9, Plaintiffs' Answer to Paddock's Counterclaims, No. 11-cv-0668, DE 12, ¶ 86 (S.D.N.Y. filed Feb. 28, 2011).

Lupin later purchased the ANTARA® rights during a bankruptcy proceeding and sold the application for its generic fenofibrate product to another manufacturer who is not marketing or selling a generic version. *Id.* ¶¶ 90–92. Although Lupin previously represented to the FDA that the '574 patent is invalid, it is now using that same patent and the related '331 patent to prevent other generic manufacturers, the Defendants, from entering the market so that Lupin can maintain its monopoly price for ANTARA®. Defendants responded to Lupin's assertion of the patents-in-suit in the same way that Lupin responded when the '574 patent was asserted against

[1] The patents-in-suit are owned by Ethypharm and allegedly licensed to Lupin Atlantis Holdings, S.A. (together, "Plaintiffs"). Ethypharm is a defendant in the Mylan, Ranbaxy, and Apotex actions, but is contractually obligated to cooperate with Lupin in its suits. Ex. 9, Plaintiffs' Answer to Paddock's Counterclaims, No. 11-cv-0668, DE 12, ¶ 77 (S.D.N.Y. filed Feb. 28, 2011).

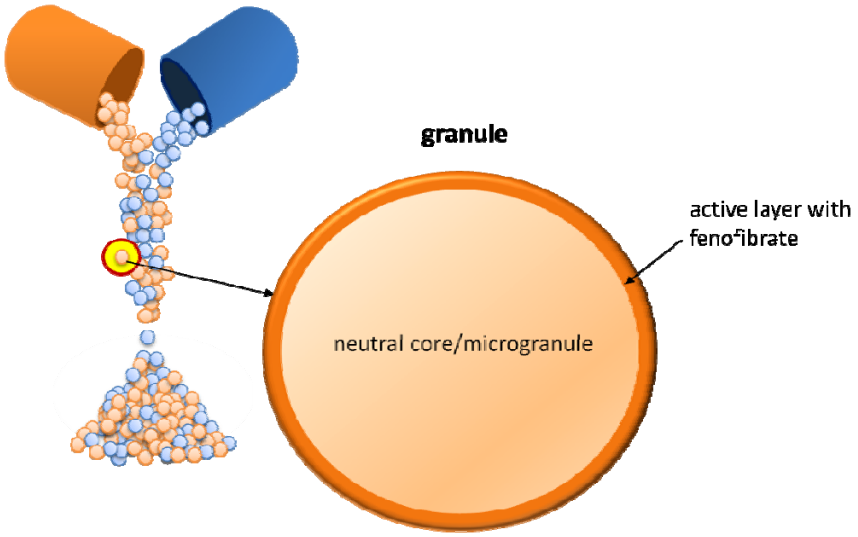
[2] All exhibits are attached to the Declaration of Charles B. Klein filed with this brief.

Lupin's proposed generic product—by alleging that the patents are invalid and would not be infringed by the proposed generic products.

THE PATENTS-IN-SUIT

The two patents-in-suit concern an active ingredient called fenofibrate, but neither claims that active ingredient itself. Fenofibrate has long been in the public domain for treating high cholesterol and triglycerides, and it is not subject to patent protection. *See* Ex. 1, '574 pat., col. 1, ll. 9–14. Since the 1980s, drug companies have developed several fenofibrate formulations. *See e.g.*, Ex. 3, U.S. Pat. No. 4,800,079.

The '574 patent covers certain fenofibrate formulations, and the '331 patent covers a method of using those formulations. Ethypharm explained during prosecution that: "The resulting granules, or coated neutral cores, are compounded for administration, e.g., in a capsule. It will be understood that each capsule would comprise a great many discrete and individual granules." Ex. 31 at 6. Ethypharm further explained: "[B]y way of illustration, the granules can be envisioned as a sphere such as an orange wherein the fruit is the neutral core and the rind is the active layer." *Id.* This description is depicted below:



'574 Patent. The '574 patent involves a "pharmaceutical composition" consisting of "granules in an amount equivalent to a dose of fenofibrate of between 50 and 300 mg." Ex. 1, '574 pat., col. 2, ll. 65–66. The granules are "prepared by assembly on neutral microgranules by spraying an aqueous solution containing the surfactant, the solubilized binding cellulose derivative and the micronized fenofibrate in suspension." *Id.* ll. 20–22. "A subject of the present invention is therefore a pharmaceutical composition containing micronized fenofibrate, a surfactant and a binding cellulose derivative, which is a solubilization adjuvant, preferably hydroxypropylmethylcellulose (HPMC)." *Id.* ll. 11–15. When the solvent evaporates, the fenofibrate, surfactant, and binding cellulose derivative are left behind on the microgranule, creating the granule.

There was nothing new about such granules. Formulations containing granules coated with fenofibrate, surfactant and a binding cellulose derivative, such as HPMC,[3] had been known for years, and were specifically disclosed in U.S. Patent No. 6,074,670 ("the '670 patent" or "Stamm"). *See* Ex. 4, '670 pat., col. 5, l. 66 – col. 6, l. 28. As a result, the '574 patent is directed toward particular weight percentages and mass ratios of the fenofibrate and binding cellulose derivative. Ex. 1, '574 pat., col. 2, ll. 32–35 ("The amount of fenofibrate is greater than or equal to 60% by weight . . . relative to the weight of the composition."); *Id.* ll. 50–52 ("The binding cellulose derivative represents between 2 and 15% . . . by weight of the composition."); *Id.* ll. 45–46 ("The fenofibrate/HPMC ratio is preferably between 5/1 and 15/1.").

The '574 patent consists of 34 claims, two of which are independent. These independent claims, claims 1 and 19, are reproduced below (with the disputed claim terms underlined):

[3] HPMC is another name for hydroxypropylmethylcellulose, which the patent describes as the preferred "binding cellulose derivative." Ex. 1, '574 pat., col. 2, ll. 13–15.

> 1. A pharmaceutical composition in the form of granules, wherein each granule comprises a neutral microgranule on which is a composition comprising: micronized fenofibrate, a surfactant, and a binding cellulose derivative as a solubilization adjuvant, and
>
> > wherein said fenofibrate is present in an amount greater than or equal to 60% by weight, relative to the weight of said pharmaceutical composition, and further wherein said binding cellulose derivative represents between 2 to 15% by weight, relative to the weight of said pharmaceutical composition.
>
> 19. A pharmaceutical composition in the form of granules, wherein each granule comprises a neutral microgranule on which is a composition comprising: micronized fenofibrate, a surfactant, and a binding cellulose derivative as a solubilization agent, wherein the mass ratio of said fenofibrate to said binding cellulose derivative is between 5/1 and 15/1.

Dependent claims 8, 16–17 and 26–30 specify an optional excipient. Dependent claims 10 and 34 recite a gelatin capsule enclosing the granules. Claim 11 recites a method of preparing the granules of claim 1. The remaining dependent claims specify the fenofibrate, the surfactant and the binding cellulose derivative used.

'331 Patent. The '331 patent was filed as a continuation-in-part of the '574 patent and is, therefore, part of the same patent family as the '574 patent.[4] The '331 patent's specification repeats the '574 patent specification's discussion of the background of the invention, the prior art, the claimed spray-coated granules, and examples, and also includes additional material.

The '331 patent claims are directed to a method of using the dosage form to treat high cholesterol, triglycerides, or lipids. The '331 patent consists of 4 claims, only one of which is independent. Independent claim 1 is reproduced below (with the disputed claim terms underlined).

[4] A continuation-in-part application, is an application in which the applicant has provided substantially the same specification as the parent application, but has disclosed additional subject matter that was not included in the parent. *See* 37 C.F.R. § 1.53(b); Ex. 10, Manual of Patent Examining Procedure § 201.08, at p. 200-53–54, July 2010 (8th ed., Rev. 8).

> 1. A method of reducing food effect when treating hypertriglyceridemias and/or hypercholesterolemias and/or hyperlipidemias in a patient in need thereof comprising administering to said patient a therapeutically effective amount of a pharmaceutical composition comprising micronized fenofibrate, a surfactant and hydroxypropylmethylcellulose,
> wherein said composition is in the form of granules comprising:
>
> (a) a neutral core; and
>
> (b) an active layer, surrounding the neutral core;
>
> wherein said neutral core comprises a sugar or a sugar mixed with starch; said active layer comprises the micronized fenofibrate, the surfactant, and the binding cellulose derivative; and wherein the mass ratio of said fenofibrate to said hydroxypropylmethylcellulose is between 5/1 and 15/1, and said hydroxypropylmethylcellulose represents between 5 and 12% by weight of the composition.

The remaining dependent claims 2–4 describe the methods of using the formulation with various diets to treat high cholesterol.

ARGUMENT

Claim construction is a matter of law for the Court. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 384–91 (1996). In *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc), the Federal Circuit set forth the pertinent legal principles governing claim construction. The Court of Appeals explained that "the words of a claim are generally given their ordinary and customary meaning," and that "the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, *i.e.*, as of the effective filing date of the patent application." *Id.* at 1312-13 (internal quotation marks omitted). "Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Id.* at 1313. "[T]he best source for understanding a technical term is the specification from which it

arose, informed, as needed, by the prosecution history." *Id.* at 1315; *accord N.Y. Univ. v. Autodesk Inc.*, No. 06-cv-5274, 2007 WL 1087202, at *1 (S.D.N.Y. Apr. 10, 2007) (Rakoff, J.).

Statements made during the prosecution of a later-filed continuation-in-part application, often called the "child," may be used to construe the claims of the earlier-filed "parent" application. This is particularly true where, as here, the patents share a specification and use the same claim terms. As the Federal Circuit explained: "Any statement of the patentee in the prosecution of a related application as to the scope of the invention would be relevant to claim construction." *Microsoft Corp. v. Multi-Tech Sys., Inc.*, 357 F.3d 1340, 1349–50 (Fed. Cir. 2004). A patentee's statements made *after* the first-filed (or parent) application issued are still relevant to construing the technology shared by the related applications. *Id.* ("[W]e conclude that [patentee's] statements made during the prosecution of the '627 patent with regard to the scope of its inventions as disclosed in the common specification are relevant not only to the '627 and '532 patents [the children], but also to the earlier issued '649 patent [the parent.]"); *Verizon Services Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1307 (Fed. Cir. 2007) ("As we held in *Microsoft*, where we faced the same situation (disclaimer occurred after patent-in-suit had issued), we think that it is not unsound to apply the same interpretation to the patent-in-suit, even though that patent had already issued.") (internal quotations removed).

The *Phillips* decision emphasizes "the importance of intrinsic evidence in claim construction," which consists of the patents and their prosecution histories. 415 F.3d at 1317 (internal quotation marks omitted). The Federal Circuit "also authorize[s] district courts to rely on extrinsic evidence, which consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises[,]" *Id.*, (internal quotation marks omitted). The parties have agreed that expert and inventor testimony is

not necessary to construe the disputed claims discussed below. Dictionaries and treatises may provide guidance where the patents are silent. *See id.*

The '574 Patent[5]

1. **"Pharmaceutical composition," "said pharmaceutical composition," and "the composition"**

"Pharmaceutical composition" (also applies to the '331 patent)

Plaintiffs' Construction	Defendants' Construction
a composition which is suitable for pharmaceutical use	all of the active and inactive ingredients in the final dosage form

"said pharmaceutical composition"

Plaintiffs' Construction	Defendants' Construction
the pharmaceutical composition in the form of granules, wherein each granule comprises a neutral microgranule on which is a composition comprising: micronized fenofibrate, a surfactant, and a binding cellulose derivative as a solubilization adjuvant/agent	all of the active and inactive ingredients in the final dosage form

"the composition" (applies to the '331 patent)

Plaintiffs' Construction	Defendants' Construction
the pharmaceutical composition comprising micronized fenofibrate, a surfactant and hydroxypropylmethylcellulose, wherein said composition is in the form of granules comprising: (a) a neutral core; and (b) an active layer	all of the active and inactive ingredients in the final dosage form

The terms "pharmaceutical composition," "said pharmaceutical composition" and "the composition" all relate to the weight percentage limitations in the patents:

- Claim 1 of the '574 patent states in relevant part: "A *pharmaceutical composition* in the form of granules . . . wherein said fenofibrate is present in an amount greater than or equal to 60% by weight, relative to the weight of *said*

[5] Related terms have been grouped together to simplify the claim construction analysis.

pharmaceutical composition, and further wherein said binding cellulose derivative represents between 2 to 15% by weight, relative to the weight of *said pharmaceutical composition*." (Emphasis added.)

- Claim 1 of the '331 patent states in relevant part: "A method of reducing food effect when treating hypertriglyceridemias and/or hypercholesterolemias and/or hyperlipidemias in a patient in need thereof comprising administering to said patient a therapeutically effective amount of a *pharmaceutical composition* comprising micronized fenofibrate, a surfactant and hydroxypropylmethylcellulose . . . wherein . . . said hydroxypropylmethylcellulose represents between 5 and 12% by weight of *the composition*." (Emphasis added.)

When referring to the "weight of *said* pharmaceutical composition" or the "weight of *the* composition," the patents are referring to the weight of all of the active and inactive ingredients in the claimed final dosage form—here, a capsule. The specification explains that the "pharmaceutical composition of the invention" is not limited to the active and other ingredients mentioned in the claims—*i.e.*, fenofibrate, a surfactant, and a binding cellulose derivative. On the contrary, as the '574 patent specification explains, the composition may include one or more other ingredients (known as excipients) not mentioned in the claims: "The *pharmaceutical composition of the invention may also contain at least one excipient* such as diluents, for instance lactose, antifoaming agents, for instance DIMETHICONE and SIMETHICONE, or lubricants, for instance talc." Ex. 1, '574 pat., col. 2, ll. 60–63 (emphasis added). *All* of the active and inactive ingredients in the claimed capsule comprise the "pharmaceutical composition" for purposes of applying the claimed weight limitations.

This point was made clear during prosecution of the patent. Ethypharm submitted a Second Declaration of George Bobotas, Ph.D. to distinguish the application's fenofibrate weight percentage limitation (greater than or equal to 60% relative to weight of the pharmaceutical composition) from the prior art. In his declaration, Dr. Bobotas explained how he determined the fenofibrate weight percentage for the prior art TRICOR® fenofibrate capsules. As the

declaration makes clear, the calculations are based on the stated amounts of ingredients when known, and the weight of the pharmaceutical composition includes *all* of the capsule's "contents," *i.e.*, all active and inactive ingredients "in each capsule":

> I supervised an analysis of the 200mg TRICOR® fenofibrate capsules to ascertain the weight percentage of fenofibrate in the formulation. *10 capsules* (Lot # 727552E21) *were opened and the contents were weighed*. *Dividing this amount by the number of capsules gave the average weight of the formulation in each capsule*. *The average weight of the formulation in each capsule* was 343 mg. Thus, assuming that each capsule contained 200 mg fenofibrate, the formulation of the 200mg TRICOR® fenofibrate capsules is about 58% fenofibrate by weight, relative to the weight of the formulation.

Ex. 25 at 2, ¶ 7 (emphasis added).

Ethypharm relied on this declaration to argue that the prior art TRICOR® fenofibrate capsules contain only "58% fenofibrate by weight, relative to the weight of the formulation[.]" Ex. 26 at 10. According to Ethypharm, these prior art capsules are "outside the instant claims," which are limited to capsules containing at least 60% fenofibrate by weight, relative to the weight of the pharmaceutical composition or formulation. *Id.* The Examiner accepted Ethypharm's argument. Ex. 27 at 8. Plaintiffs cannot now reverse course and argue that the "pharmaceutical composition" is anything other than the capsule's "contents," *i.e.*, *all* of the active and inactive ingredients in the final dosage form. *See Phillips*, 415 F.3d at 1317 ("[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention[.]").

2. "granule" and "active layer"

"granule"

Plaintiffs' Construction	Defendants' Construction
neutral microgranule on which there is a mixture of micronized fenofibrate, a surfactant, and a binding cellulose derivative as a solubilization adjuvant/agent	neutral microgranule on which is sprayed a suspension of micronized fenofibrate, a surfactant, and a binding cellulose derivative as a solubilization adjuvant/agent

"active layer" (applies to the '331 patent)

Plaintiffs' Construction	Defendants' Construction
a mixture of micronized fenofibrate, a surfactant, and hydroxypropylmethylcellulose	layer comprised of micronized fenofibrate, surfactant, and binding cellulose derivative sprayed on the outside of the neutral core

The main difference between the parties' constructions of these two terms is that Defendants' construction clarifies that the suspension of micronized fenofibrate, a surfactant and a binding cellulose derivative is *sprayed* onto the neutral microgranule. This requirement is supported by the inventors' statements both in the patents and during prosecution.

The application that led to the '574 patent described two methods of forming granules: spraying and wet granulation of powder. The specification describes both methods, and the original claims claimed each separately. Ex. 17 at 5–6 (reciting claim 12 describing spray-coating method and claim 13 describing wet granulation). But after four rejections and an interview, the inventors disclaimed the wet-granulation method because it was widely known in the prior art. Ex. 22 at 3 ("Applicants will further amend claim 1 to recite a granule form . . . . Claims 38-46 will be canceled without prejudice."); Ex. 24 at 9 ("It was further agreed [in the interview] that patentability would be further supported by amendments reciting that the claimed composition is in granule form"); Ex. 23 at 2–8 (canceling wet granulation method and limiting all remaining claims to granule form).

This left just *one* claimed method for preparing the claimed granules, *i.e.*, spraying the fenofibrate mixture onto the neutral microgranule or core. The specification for the '574 patent explains this spraying method for preparing a "granule":

> The composition of the invention is advantageously provided as gelatin capsules containing . . . granules[.] . . . *These granules may in particular be prepared by assembly on neutral microgranules, by spraying an aqueous solution containing the surfactant, the solubilized binding cellulose derivative and the micronized fenofibrate in suspension*.

Ex. 1, '574 pat., col. 2, ll. 18–22 (emphasis added). The inventors repeatedly defined "granules" in this manner throughout the specification. *See id.*, col. 3, ll. 12–15 ("The assembly of neutral microgranules is carried out *by spraying* an aqueous suspension containing the surfactant, the solubilized binding cellulose derivative, and the micronized fenofibrate in suspension.") (emphasis added); *id.*, col. 3, ll. 55–56 ("The microgranules are obtained *by spraying* an aqueous suspension onto neutral cores.") (emphasis added); *id.*, col. 4, ll. 23–24 (same). Every recited example of the claimed formulation is created by spraying.[6] *See Edward Lifesciences LLC v. Cook Inc.*, 582 F.3d 1322, 1330 (Fed. Cir. 2009) ("[W]hen the preferred embodiment is described in the specification as the invention itself, the claims are not necessarily entitled to a scope broader than that embodiment.") (internal citations omitted); *Verizon*, 503 F.3d at 1308 ("When a patent . . . describes the features of the 'present invention' as a whole, this description limits the scope of the invention.").

The '574 patent itself claims only one method—the spraying method—for creating the granules. Ex. 1, '574 pat., claim 11 ("A method for preparing the pharmaceutical composition of claim 1, wherein said granules are *prepared by spraying onto neutral microgranules*. . . ."). In fact, the inventors distinguished prior art on the ground that the patent did *not* claim products formed by the alternative, wet-granulation method: "EP 958 [prior art] is limited to a fenofibrate formulation fabricated by wet granulation. The wet granulation method produces an irregular mixture lacking the finely layered structure of microscrystalline fenofibrate on an inert core [prepared through the spraying method], which is a characteristic of Boyer '079 and *the present invention*." Ex. 28 at 10 (emphasis added); *see also Fantasy Sports Properties, Inc. v.*

[6] Ex. 1, '574 pat., Example 1A, col. 3, ll. 49–66 ("The microgranules are obtained by spraying an aqueous suspension of micronized fenofibrate onto neutral cores."); Example 1B, col. 4, ll. 20–41 ("The microgranules are obtained by spraying an aqueous suspension onto neutral cores.").

Sportsline.com, Inc., 287 F.3d 1108, 1115-16 (Fed. Cir. 2002) (where the patent applicant disclaimed subject matter during prosecution in order to obtain the patent, the patentee cannot attempt to recapture that subject matter through the doctrine of claim differentiation). And Plaintiffs cannot now assert that claim 1 covers any other method of creating granules not included in the specification because any such method would not be enabled. *See Alza Corp. v. Andrx Pharma., LLC*, 603 F.3d 935, 941 (Fed. Cir. 2010) ("To satisfy the plain language of § 112, ¶ 1, [patentee] was required to provide an adequate enabling disclosure in the specification; it cannot simply rely on the knowledge of a person of ordinary skill to serve as a substitute for the missing information in the specification.").

The specification of the '331 patent discloses *only* the spraying method for getting the active layer on the neutral core. The specification discusses that spraying method for creating granules three times. Ex. 2, '331 pat., col. 2, ll. 38–51; col. 3, ll. 15–20 ("These granules may in particular be prepared by assembly on neutral cores, *spraying* an aqueous solution containing the surfactant, the solubilized binding cellulose derivative and the micronized fenofibrate in suspension.") (emphasis added); col. 6, ll. 9–13 ("The assembly on neutral cores is carried out by *spraying* an aqueous solution containing the surfactant, the solubilized binding cellulose derivative, and the micronized fenofibrate in suspension.") (emphasis added); *see also id.* col. 2, ll. 48–51 (Thus, when the solvent is removed from the suspension by evaporation *after spraying onto neutral cores*, molecules of both cellulose derivative and surfactant are absorbed directly onto the fenofibrate microparticles.") (emphasis added). No reference to any other method of preparation was included in the application underlying the '331 patent. *See generally* Ex. 30.

Plaintiffs cannot now seek to recapture subject matter, *i.e.*, alternative methods for preparing granules, they clearly ceded during prosecution of the two patents. Ethypharm's

representations during prosecution show how the "inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Phillips*, 415 F.3d at 1317; *MBO Labs., Inc. v. Becton, Dickenson & Co.*, 602 F.3d 1306, 1318 (Fed. Cir. 2010) ("[T]his court reviews a patent family's entire prosecution history when applying both the rule against recapture and prosecution history estoppel. . . . '[B]oth operate . . . to prevent a patentee from encroaching back into territory that had previously been committed to the public.'") (quoting *MBO Labs., Inc. v. Becton, Dickenson & Co.*, 474 F.3d 1323, 1332 (Fed. Cir. 2007)). The terms "granules" and "active layer" are thus best construed as requiring the fenofibrate suspension be *sprayed* onto the outside of the neutral microgranule or core.

3. "granules" (applies to both patents)

Plaintiffs' Construction	Defendants' Construction
neutral microgranules on which there is a mixture of micronized fenofibrate, a surfactant, and a binding cellulose derivative as a solubilization adjuvant/agent	many discrete granules

The plural term "granules" obviously refers to more than one "granule." Here, Ethypharm acted as its own lexicographer to clarify that using only two or three granules will not suffice. Instead, the term "granules" in this context refers to *many* discrete granules: "It will be understood that each capsule would comprise a great *many discrete and individual granules*." Ex. 31 at 6 (emphasis added); *see also Edward Lifesciences*, 582 F.3d at 1329 ("[W]e will adopt a definition that is different from the ordinary meaning when 'the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in either the specification or prosecution history.'") (quoting *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366–67 (Fed. Cir. 2002)).

The above statement by the inventors to the Patent Office "inform[s] the meaning of the claim language by demonstrating how the inventor understood the invention." *Phillips*, 415 F.3d at 1317. Although this statement comes from the prosecution history of the '331 patent (the child), it informs the meaning of the term in both patents. Ethypharm represented to the Patent Office that the basic pharmaceutical composition "in the form of granules" described in both the parent and child patents is the same:

> Applicants invite the Office's attention to related U.S. Patent No. 7,101,574, as to which Applicants have submitted a Terminal Disclaimer. The claims of the '574 patent are directed to a distinct yet analogous invention. *There, as here, the claims include reference to a pharmaceutical composition in the form of granules having an active layer coating a neutral core.*

Ex. 32 at 10 (emphasis added). Ethypharm itself thus confirmed that the claim term "granules" has the same meaning in both the '331 and '574 patents. And that meaning is "a great many discrete and individual granules." That definition offered by the inventors themselves should be the meaning of the term "granules" in both the parent '574 patent and the child '331 patent. *See Microsoft*, 357 F.3d at 1350 ("We take the patentee at its word and will not construe the scope of the [earlier-issued] patent's claims more broadly than the patentee itself clearly envisioned.").

Defendants simply shortened Ethypharm's own construction to "many discrete granules." The invention here—according to the inventors themselves—requires many discrete granules and not alternative formulations.

4. "each granule"

Plaintiffs' Construction	Defendants' Construction
no additional construction necessary	each and every granule in the pharmaceutical composition contains all the required ingredients

"Each granule," as used in claims 1 and 19, should be construed to mean that "each and every granule in the pharmaceutical composition contains all the required ingredients."

First, the plain language of the claims requires that each granule contain all of the required ingredients, otherwise the reference to "each" granule would be meaningless. *See Phillips*, 415 F.3d at 1314 (citing *Vitronics*, 415 F.3d at 1314) ("The claims themselves provide substantial guidance as to the meaning of particular claim terms"). Plaintiffs' failure to give any meaning to this explicit language choice is plainly wrong under Federal Circuit law. *See Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 950 (Fed. Cir. 2006) ("[C]laims are interpreted with an eye toward giving effect to all terms in the claim").

Second, the patent specification uses "each" in its ordinary and customary manner to refer to "every single one." For example, the specification states that "[t]he microgranules obtained are distributed into size 1 gelatin capsules, *each* containing 200 mg of fenofibrate." Ex. 1, '574 pat., col. 4, ll. 60–61 (emphasis added). This statement means that every gelatin capsule has the recited amount of fenofibrate. Thus, the specification confirms that the word "each" was used in the patent in its ordinary and customary manner.

Third, the '574 patent specification is clear that each and every granule in the pharmaceutical composition contains all the required ingredients. Indeed, the specification consistently teaches that the individual granules are prepared in the same manner and contain all the recited ingredients. *Id.* col. 3, ll. 50–67; *id.* col. 6, ll. 49–60.

Fourth, the prosecution history further confirms Defendants' construction. Significantly, the "each granule" limitation was not present in the original version of the asserted claims and was added to overcome prior art which allegedly did not disclose that each granule contained the recited ingredients. *Compare* Ex. 20 at 1, 6 *with* Ex. 23 at 2, 5. Nor was this a mere stylistic clarifying amendment. The patentee expressly conceded that this amendment was for

patentability reasons. Ex. 24 at 9 ("It was further agreed that patentability would be further supported by amendments reciting that the claimed composition is in granule form . . . .").

Fifth, the Federal Circuit and numerous district courts have repeatedly and consistently construed "each" as meaning "each and every." *E.g.*, *ResQNet.com, Inc. v. Lansa, Inc.*, 346 F.3d 1374, 1379 (Fed. Cir. 2003) (stating that the term "each" means each and every); *Medtronic, Inc. v. Guidant Corp.*, Nos. 00-1473, 00-2503, 2004 WL 1179338, at *42 (D. Minn. May 25, 2004) (construing "each" to mean "every one of two or more considered individually or one by one"); *Genlyte Thomas Group LLC v. Lutron Elecs. Co.*, No. 3:02-cv-602-K, 2004 WL 690847, at *5 (N.D. Tex. Mar. 31, 2004) (construing each as "every" when it is used as an adjective).

Thus, Defendants' construction of each granule should be adopted because it closely aligns with the specification, prosecution history, and the customary meaning of "each."

5. "neutral microgranule" and "neutral core"

"neutral microgranule"

Plaintiffs' Construction	Defendants' Construction
a therapeutically neutral substrate or region of a substrate	sugar or sugar mixed with starch particle having a size of between 200 and 1,000 microns and containing no fenofibrate

"neutral core" (applies to the '331 patent)

Plaintiffs' Construction	Defendants' Construction
a pharmaceutically neutral substrate to which active layer can be applied	same as neutral microgranule

Defendants' construction of "neutral microgranule" and "neutral core" can be subdivided into two discrete elements:

(1) a size limitation (*i.e.*, particle having a size between 200 and 1,000 microns), and

(2) a composition limitation (*i.e.*, sugar or sugar mixed with starch particle [in contrast to a particle containing starch alone]. . . containing no fenofibrate).

Each element is amply supported by the patent and prosecution history.

First, the inventors expressly imposed a size limitation for a "neutral microgranule" or "neutral core" in both patent specifications: "*The neutral microgranules have a particle size of between 200 and 1,000 microns*, preferably between 400 and 600 microns." Ex. 1, '574 pat., col. 3, ll. 6–15 (emphasis added); Ex. 2, '331 pat., col. 6, ll. 1–2 ("The neutral cores have a particle size of between 200 and 1,000 microns, preferable between 400 and 600 microns.").[7] The '574 patent specification devotes an entire paragraph to this single, unambiguous sentence. The only other mention of the size limitation is in Example 1B, where the neutral microgranules are within the preferred disclosed range: "The size of the neutral microgranules is between 400 and 600 [microns]." Ex. 1, '574 pat., col. 3, ll. 41–42; Ex. 2, '331 pat., col. 7, l. 11 ("The size of the neutral cores is between 400 and 600 [microns].").

Limiting a "neutral microgranule" to particles between 200 and 1,000 microns thus defines the term "in a way that comports with the instrument as a whole." *Markman*, 517 U.S. at 389. Indeed, the Court "cannot construe the claims to cover subject matter broader than that which the patentee itself regarded as comprising its inventions and represented to the PTO." *Microsoft*, 357 F.3d at 1349.

This size limitation also comports with the plain meaning of "neutral microgranule" in the art, as evidenced by the prosecution history of the patent family. The plain meaning of a *micro*granule, by definition, is "very small"—*i.e.*, smaller than a granule Ex. 11, "micro," Merriam-Webster's Medical Dictionary (2007), *available at* http://dictionary.reference.com/browse/micro. Indeed, prior art disclosed by Ethypharm discussed similar particles measuring less than 1,000 microns (or 1 mm) that are coated with

[7] A micron is also called a micrometer (abbreviated μm); 1,000 microns is equal to 1 millimeter. Ex. 12, "micron," Merriam-Webster's Medical Dictionary (2007), *available at* http://dictionary.reference.com/browse/micron.

active ingredients.[8] During prosecution of the '331 patent, Ethypharm represented that "[n]eutral cores are well known and widely used within the pharmaceutical arts, and are generally understood to be about 200 to about 1000 microns in diameter." Ex. 31 at 6. This history confirms that one skilled in the art at the time of the invention would read "neutral microgranule," particularly in the context of the '574 patent's claims and specification, to refer to a particle having a size of between 200 and 1,000 microns.

The Court should read "neutral microgranule" synonymously with the term "neutral core" because the inventors used both terms interchangeably throughout the specification of the '574 patent. *Compare* Ex. 1, '574 pat., col. 3, ll. 11–14 ("The assembly of *neutral microgranules* is carried out by spraying an aqueous suspension containing the surfactant, the solubilized binding cellulose derivative, and the micronized fenofibrate in suspension.") (emphasis added), *with id.*, col. 3, ll. 55–56 ("The microgranules are obtained by spraying an aqueous suspension onto *neutral cores*.") (emphasis added) *and id.* col. 4, ll. 23-24 (same). "The interchangeable use of the two terms is akin to a definition equating the two." *Edward Lifesciences*, 582 F.3d at 1329 (holding interchangeable use of two terms functioned as patentee acting as its own lexicographer).

The inventors carried the term "neutral core" over to the claims of the '331 patent from the shared specification. In fact, Ethypharm treated "neutral microgranules" and "neutral cores" as synonyms during prosecution of the '331 patent: "The claims of the '574 patent are directed

[8] *See e.g.*, Ex. 3, U.S. Pat. No. 4,800,079 (disclosed in Ethypharm's Second IDS, Feb. 20, 2003) ("Inert grains for forming the inert cores are prepared in conventional manner. For example, each grain may be a sucrose crystal having a diameter of 0.3 mm [300 microns]."); Ex. 5, Foreign Pat. No. WO 98/00116, p.4, ll. 18–29 (disclosed in Ethypharm's First IDS, Jan. 8, 2002) ("The beads or seeds are discrete particles, . . . which serve as the solid substrate upon which the antifungal compound is coated . . . Beads of differing mesh sizes can be employed. . . Such mesh sizes refer to particle or bead sizes whose diameters can ranges from about 1.0 millimeters (mm) [1,000 microns] to about 0.297 mm [297 microns].").

to a distinct yet analogous invention. There, *as here*, the claims include reference to a pharmaceutical composition in the form of granules having an active layer coating a *neutral core*." Ex. 32 at 10 (emphasis added); *compare* Ex. 1, '574 pat., claim 1, col. 10, ll. 29–32. ("each granule comprises a *neutral microgranule* on which is a composition comprising: micronized fenofibrate, a surfactant, and a binding cellulose derivative as a solubilization adjuvant") (emphasis added). Plaintiffs have no basis to offer different constructions for these two terms—they mean the exact same thing.

Second, the inventors considered a "neutral microgranule" and a "neutral core" to be a particle made of sugar or sugar mixed with starch and not containing fenofibrate. The "neutral microgranule" or "neutral core" could not be made of other inert substances in the absence of any sugar, such as starch alone.

Both sides agree that the neutral microgranule/neutral core is therapeutically neutral (or inert), *i.e.*, it does *not* contain the active ingredient fenofibrate. The pertinent dispute concerns what *is* contained in this neutral core. To resolve this dispute, the Court has to look no further than claim 1 of the '331 patent itself, which says that "*said neutral core comprises a sugar or sugar mixed with starch [particle]*." Ex. 2, '331 pat., claim 1, col. 16, ll. 59–60 (emphasis added). The inventors offered no other definition for neutral microgranule or neutral core.

The prosecution history confirms the inventors' view that the composition of the neutral microgranule or core must contain sugar. In distinguishing prior art, Ethypharm compared the '574 patent to its own prior patent on micronized fenofibrate compositions with "inert cores." Ex. 28 at 9–10 ("The wet granulation method produces an irregular mixture lacking the finely layered structure of microcrystalline fenofibrate on an inert core, *which is a characteristic of Boyer '079 and the present invention*.") (emphasis added). The Boyer patent, U.S. Pat. No.

4,800,079, assigned to Ethypharm in 1989, describes inert cores "prepared in [the] conventional manner." Ex. 3, '079 pat., col. 2, ll. 38–39. This "conventional manner" is described as taking a sugar crystal and coating it with a mixture of sugar and starch to achieve the desired particle size. *Id.* col. 2, ll. 38–51.

Other prior art cited in the prosecution history confirms that one skilled in the art at the time of the invention would understand a neutral microgranule (or neutral core) to be comprised of a sugar or a sugar mixed with starch particle.[9] In fact, coated granules directly descended from sugar sprinkles used on desserts:

> A major breakthrough occurred in 1949 when a pharmaceutical scientist . . . realized the potential application of candy seeds in sustained-release preparations and embarked on the development of tiny drug pellets that could be loaded into capsules. The candy seeds were nothing but small sugar particles that were used for topping decorations on pastries and related foodstuffs. . . . [T]he candy seeds or nonpareils, which are inert and innocuous, functioned as starter seeds upon which drugs were layered.

Ex. 13, Isaac Ghebre-Sellassie, Pellets: A General Overview, *in Pharmaceutical Pelletization Technology*, 1, 4 (Isaac Ghebre-Sellassie ed., 1989) (disclosed in Ethypharm's Fifth IDS Oct. 21, 2005). A skilled artisan thus would understand the claimed neutral microgranule or core to contain sugar, as confirmed by the inventors themselves in claim 1 of the '331 patent.

[9] *E.g.*, Ex. 6, Foreign Pat. No. WO 82/01649, Abstract, p. 1 (disclosed in Ethypharm's Fifth IDS, Oct. 21, 2005) ("The medicine is formed with granules, each of them being comprised of a neutral core (saccharose + starch) covered with a first layer of phenofibrate"); Ex. 7, Foreign Pat. No. EP 0 793 958 A2, p. 4 (disclosed in Ethypharm's Fifth IDS, Oct. 21, 2005) (transl. from German by Ethypharm) ("Moreover, drugs are known . . . containing an active-substance layer with binding agents and containing a water-permeable, porous jacketing whose *neutral core consists of inert binding agents selected from the group of raw sugar and lactose, optionally starch*, and in which the neutral core is jacketed with a first layer containing active substance containing fenofibrate.") (emphasis added).

6. "micronized fenofibrate" (applies to both patents)

Plaintiffs' Construction	Defendants' Construction
fenofibrate that has a smaller particle size than non-micronized fenofibrate such that it exhibits enhanced solubility and/or rate of solubilization when compared to non-micronized fenofibrate	fenofibrate particles of a size less than 15 microns free of other ingredients when micronized, and present in an aqueous suspension with one or more other ingredients when coated on the neutral core or neutral microgranule

The claims of the '574 and '331 patents are directed to a pharmaceutical composition comprising, *inter alia,* micronized fenofibrate. Claim 1 of the '331 patent claims "an active layer, surrounding the neutral core . . . said active layer comprises the micronized fenofibrate. . . ."

Defendants' proposed definition of micronized fenofibrate comes directly from the '574 and '331 patent specifications, where the patentee specifically defined "micronized fenofibrate" to have a mean size of less than 15 microns. Ex. 1, '574 pat., col. 2, ll. 58–59 ("The mean size of the fenofibrate particles is less than 15 µm, preferably 10 µm, even more preferably less than 8 µm."); Ex. 2, '331 pat., col. 4, ll.13–14 (same). The specification here is unequivocal: the mean particle size of the micronized fenofibrate must be less than 15 microns, and an even small size in preferred embodiments—10 microns and even more preferably less than 8 microns. *Id.*

The specification explains the reason for needing a small particle size—namely, to provide a "high proportion of fenofibrate" that allows for the fenofibrate to be "provided in a formulation that is smaller in size than the formulations of the prior art, which makes this composition according to the invention easy to administer." *See SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1341 (Fed. Cir. 2001) ("Where the specification makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims of the patent, even though the language of the

claims, read without reference to the specification, might be considered broad enough to encompass the feature in question."); *Watts v. XL Sys.*, 232 F.3d 877, 882 (Fed. Cir. 2000) ("One purpose for examining the specification is to determine if the patentee has limited the scope of the claims.")

Defendants' proposed definition also reflects the inventors' additional requirement that the fenofibrate be "micronized alone"—free of other ingredients—because the '574 and '331 patent specifications explicitly disclaim the fenofibrate being micronized with any other ingredients:

> *In the context of the present invention*, the fenofibrate is not comicronized with a surfactant. On the contrary, it *is micronized alone* and then combined with a surfactant and with the binding cellulose derivative, which is a solubilization adjuvant.

Ex. 1, '574 pat., col. 2, ll. 36–40 (emphasis added); Ex. 2, '331 pat., col. 3, ll. 58–62 (same).

Again, the specification is unequivocal. The micronized alone requirement "[i]n the context of the present invention," is not an optional embodiment. *See Honeywell Int'l v. ITT Indus.*, 452 F.3d 1312, 1318 (Fed. Cir. 2006) (defining claims in way that the specification described as "the invention.").

This limitation was also relied upon in an attempt to distinguish the claimed fenofibrate from prior art disclosures of micronized fenofibrate where the fenofibrate is micronized with other ingredients, such as a surfactant:

> Patent EP 330 532 proposes improving the bioavailability of fenofibrate by comicronizing it with a surfactant, such as sodium lauryl sulfate. The comicronizate is then granulated by wet granulation in order to improve the flow capacities of the powder and to facilitate the transformation into gelatin capsules. This comicronization allows a significant increase in the bioavailability compared to the use of fenofibrate described in EP 256 933. The granules described in EP 330 532 contain polyvinylpyrrolidone as a binder.

> *This patent teaches that the comicronization of fenofibrate with a solid surfactant significantly improves the bioavailability of the fenofibrate compared to the use of a surfactant, of micronization or of the combination of a surfactant and of micronized fenofibrate.*

Ex. 1, '574 pat., col. 1, ll. 39–53(emphasis added); Ex. 2, '331 pat., col. 1, l. 61 – col. 2, l. 7 (same); *see O.I. Corp. v. Tekmar Co.*, 115 F.3d 1576, 1581 (Fed. Cir. 1997) (limiting claims because the specification described only non-smooth or conical passages and distinguished over the prior art based on these characteristics).

Defendants' definition further reflects the specifications' statements that micronized fenofibrate is present in an aqueous suspension containing the micronized fenofibrate, the surfactant and the solubilized binding cellulose derivative that is coated on the neutral core. Ex. 1, '574 pat., col. 3, ll. 11–14 ("The assembly of neutral microgranules is carried out by spraying an aqueous suspension containing the surfactant, the solubilized binding cellulose derivative, and the micronized fenofibrate in suspension."); Ex. 2, '331 pat., col. 6, ll. 9–13. In other words, the micronized fenofibrate is only joined with other ingredients as part of the suspension that is being applied to the core *after* it has been micronized.

This requirement was confirmed during prosecution. Following cancellation of the claims to wet granulation, as discussed in section 2, Ethypharm explained how the process of this invention differed from other processes such as wet granulation when attempting to overcome a prior art reference. Ex. 28 at 12 ("One of ordinary skill in the art would have understood from EP 958 that materials said to be beneficial – perhaps even necessary – in a wet granulation formulation are not beneficial – and perhaps must be excluded – in a neutral core formulation."). How the micronized fenofibrate is applied to core is explained in greater detail in section 2 defining "granule" and "active layer."

Therefore, the term "micronized fenofibrate" should be construed as "fenofibrate particles of a size less than 15 microns that are free of other ingredients when micronized, and present in an aqueous suspension when coated on the neutral core or neutral microgranule."

7. **"surfactant"** (applies to both patents)

Plaintiffs' Construction	Defendants' Construction
a substance that lowers the surface tension of water	An amphiphilic, surface-tension lowering substance, that when present in a sufficient amount and under appropriate conditions, increases the bioavailability of fenofibrate, and does not include anti-foaming agents such as simethicone

Both Plaintiffs and Defendants agree that one of the features of a surfactant is that it reduces the surface tension of water. However, not every substance that lowers the surface tension of water is necessarily a surfactant. Other required elements in the claimed composition, such as a cellulose derivative like HPMC, which is discussed extensively in the specification but never defined as a "surfactant," also would have the effect of reducing surface tension in water. *See* Ex. 14, DOW, METHOCEL CELLULOSE ETHERS TECHNICAL HANDBOOK, 3, 16 (2002) (showing that METHOCEL cellulose products lower the surface tension of water). Plaintiffs' construction omits three critical aspects of the term "surfactant" that flow from both the intrinsic record and relevant extrinsic evidence:

- The surfactant must be amphiphilic, meaning that it has a region that is attracted to water (hydrophilic) and a separate region that repels water (hydrophobic);
- "Surfactant" does not include anti-foaming agents such as simethicone. Notably, the patentee explicitly distinguished between surfactants and anti-foaming agents and *separately claimed* simethicone in dependent claim 17 as something that is used *in addition to* the surfactant. *See Phillips*, 415 F.3d at 1315 ("[T]he presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim"); and
- The surfactant must be present in a sufficient amount and under appropriate conditions to increase the bioavailability of fenofibrate, a feature that is expressly described in the

specification as the purpose for using the surfactant.

Defendants' construction gives life to these critical features, while Plaintiffs' over-simplification ignores them and seeks to impermissibly expand the scope of the claimed invention. Thus, Defendants' construction should be adopted. *See id.* at 1316 ("[T]he interpretation to be given to a term can only be determined and confirmed with a full understanding of what the inventors *actually invented* and intended to envelop with the claim.") (emphasis added; citations omitted).

First, the "surfactant" must be amphiphilic. Prior art cited by the inventors directly confirms this aspect of the definition. Ex. 5, Foreign Pat. No. WO 98/00116, p. 5 (disclosed in Ethypharm's First IDS, Jan. 8, 2002) (noting that surfactants "contai[n] two localized regions, one being *hydrophilic in nature* and the other hydrophobic") (emphasis added). Moreover, the amphiphilic feature is commonly included in definitions of surfactants because it explains the mechanism of how they work and distinguishes surfactants from other compounds that might have the effect of reducing surface tension. By being amphiphilic, a sufactant is able to reduce surface tension in water and bring a solute, here fenofibrate, into solution. *See* Ex. 15, REMINGTON: THE SCIENCE & PRACTICE OF PHARMACY 229 (Paul Beringer, et al. eds., 21st ed. 2005) (defining surfactant as "molecules with well defined polar [hydrophilic] and non-polar [hydrophobic] regions that allow them to aggregate in solution to form micelles.").

Second, "surfactant" does not include anti-foaming agents such as simethicone. The inventors drew a clear distinction in the specifications between surfactants and anti-foaming agents by repeatedly and consistently differentiating between the two. *E.g.*, Ex. 1, '574 pat., col. 2, ll. 41–45 ("The surfactant is chosen from surfactants which are solid or liquid at room temperature, for example sodium lauryl sulfate, Polysorbate® 80 or Montane® 20, preferably sodium lauryl sulfate"); Ex. 2, '331 pat., col. 3, ll. 63–67; Ex. 1, '574 pat., col. 2, ll. 60-63 ("The

composition of the invention may also contain at least one excipient such as diluents, for instance, lactose, anti-foaming agents, for instance DIMETHICONE and SIMETHICONE, or lubricants, for instance talc"); Ex. 2, '331 pat., col. 4, ll. 15–25. Additionally, both patents include examples which contain *both* an anti-foaming agent and a surfactant. Ex. 1, '574 patent, col. 4, ll. 50–55 (Example 1C containing 3.5% surfactant and 0.2% anti-foaming agent); Ex. 2, '331 patent, col. 7, ll. 51–60 (same).

Where, as here, the patentee has used terms throughout the specification to refer to different things, the terms cannot be construed to avoid that distinction. *See Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 807 (Fed. Cir. 2007) (where patentee used phrases "transverse" and "perpendicular" differently throughout the written description, while specifically using "transverse" in the claims, the Federal Circuit rejected a proffered construction that equated "transverse" to "perpendicular").

Additionally, the specification and prosecution history confirm the distinction between surfactants and anti-foaming agents. The specifications give several examples of surfactants, but never identifies anti-foaming agents as being encompassed within the term. *See e.g.* Ex. 1, '574 pat., col. 2, ll. 41–44 ("The surfactant is chosen from surfactants which are solid or liquid at room temperature, for example sodium lauryl sulfate, Polysorbate® 80 or Montane® 20, preferably sodium lauryl sulfate."). Rather, the patent consistently refers to antifoaming agents as excipients, not surfactants—specifically claiming them as such in claim 8. Thus, for example, claim 1 of the '574 patent recites a composition containing the following ingredients: (1) micronized fenofibrate (2) a surfactant and (3) a binding cellulose derivative. Ex. 1, '574 pat., col. 10, ll. 28–38. Claim 8, which depends from claim 1, adds the further limitation that the composition contains an excipient, which is expressly defined in the specification as "diluents . .

. *antifoaming agents, for instance DIMETHICONE and SIMETHICONE . . . .*" *Id.* col. 2, ll. 60–64 (emphasis added).

Additionally, claim 16, which depends from claim 8, recites that the "excipient is selected from the group consisting of a diluent, an antifoaming agent, a lubricant, and a mixture thereof." *Id.* col. 11, ll. 18–21. Claim 17 further expressly recites simethicone (specifically recited as a mixture of α-(trimethylsilyl)-ω-methylpoly[oxy-(dimethylsilylene)] with silicon dioxide). Ex. 16, Handbook of Pharmaceutical Excipients p. 652 (providing formula of simethicone). Because anti-foaming agents are separately recited in claims 8, 16, and 17 as specific examples of excipients, not surfactants, they presumptively do *not* fall within the meaning of "surfactant" in claim 1. *See Edwards Lifesciences LLC v. Cook Inc.*, 582 F.3d 1322, 1330 (Fed. Cir. 2009) (quoting *Nystrom v. TREX Co.*, 424 F.3d 1136, 1143 (Fed. Cir. 2005) ("'When different words or phrases are used in separate claims, a difference in meaning is presumed.'").

Extrinsic evidence also confirms Defendants' construction. For example, the Handbook of Pharmaceutical Excipients ("the Handbook") specifically lists the functional categories for simethicone as "anti-foaming agent; tablet diluent; water-repelling agent." Ex. 16, Handbook of Pharmaceutical Excipients p. 652 (5th ed. 2006). By contrast, the Handbook specifically lists the functional properties of sodium lauryl sulfate, the preferred surfactant in the asserted patents, as "*anionic surfactant*; detergent; emulsifying agent; skin penetrant; tablet and capsule lubricant; wetting agent." *Id.* at 687. Extrinsic evidence thus confirms that persons of ordinary skill in the art simply do not equate surfactants with anti-foaming agents.

Third, the intrinsic record also consistently emphasizes the critical role of the surfactant in increasing the bioavailability of fenofibrate and confirms that the surfactant must be present in a sufficient amount to render the fenofibrate more bioavailable. As the patentee explained in the

specification, "[f]enofibrate is an active principle which is very poorly soluble in water, and the absorption of which in the digestive tract is limited." Ex. 2, '331 pat., col. 1, ll. 26–28. Thus, *the entire problem that the patentee sought to solve was to improve the solubilization / bioavailability of fenofibrate*. *Id.* col. 2, ll. 28–35; *see Apple Computer, Inc. v. Articulate Sys., Inc.*, 234 F.3d 14, 25 (Fed. Cir. 2000) ("[T]he claim must be interpreted in light of the teachings of the written description and the purpose of the invention described therein").

The specification highlights the importance of the surfactant to this increased bioavailability. For example, the Abstract of the '574 patent states, "[t]he association of micronized fenofibrate with a binding cellulose derivative, as solubilizing adjuvant *and a surfactant enables enhanced bioavailability of the active principle*." Ex. 1, '574 patent, Abstract (emphasis added). The specification of the '331 patent also identifies the surfactant as integral to increased bioavailability in the claimed formulation:

> [W]hen the solvent is removed from the suspension by evaporation after spraying onto neutral cores, molecules of both cellulose derivative and surfactant are adsorbed directly onto the fenofibrate microparticles. . . . *[T]hese molecules, which are responsible for its better solubilization into the gastro-intestinal fluids and thereby allow a better absorption of fenofibrate* . . . .

Ex. 2, '331 pat., col. 2, ll. 47–55.

These unequivocal statements linking the increased bioavailability to the presence of the surfactant compel the conclusion that the surfactant must result in increased bioavailability.

8. "binding cellulose derivative as a solubilization adjuvant/agent"

Plaintiffs' Construction	Defendants' Construction
a cellulose-based polymer in said pharmaceutical composition that binds the micronized fenofibrate to the neutral microgranule and increases the micronized fenofibrate's solubility and/or rate of solubilization	any and all water-soluble cellulose-based polymer, such as HPMC, in the pharmaceutical composition that is capable of binding micronized fenofibrate to the neutral microgranule and increasing the micronized fenofibrate's solubility or rate of solubilization

Both independent claims of the '574 patent require a "binding cellulose derivative as a solubilization adjuvant [or agent]." The parties generally agree on which ingredients in the formulation constitute the "binding cellulose derivative as a solubilization adjuvant/agent."[10] The parties' constructions differ in two ways. First, the parties disagree as to whether a portion of such an ingredient may be disregarded when calculating the weight percent and ratio of "said binding cellulose derivative" in the "pharmaceutical composition."[11] Second, the parties disagree as to whether the cellulose-based polymer must be water soluble.

The patent specification and prosecution history make it clear that the weight of *all* cellulose derivative that is capable of acting as a binder and as a solubilization adjuvant/agent is included in the calculation. Accordingly, the phrase "binding cellulose derivative as a solubilization adjuvant" should be construed as "any and all water-soluble cellulose derivative, such as HPMC, in the pharmaceutical composition that is capable of binding pharmaceutical ingredients and increasing the micronized fenofibrate's solubility or rate of solubilization in

[10] The parties' proposed constructions reflect agreement that a "cellulose derivative" is a "cellulose-based polymer," although they disagree as to whether it is appropriate to include the exemplary phrase, "such as HPMC." The proposed constructions also reflect agreement that the terms "solubilization adjuvant" and "solubilization agent" have the same meaning, and refer to increasing micronized fenofibrate's solubility or rate of solubilization.

[11] As discussed in more detail below, Claim 1 of the '574 patent requires the binding cellulose derivative is present in an amount between 2 to 15% by weight relative to the weight of the pharmaceutical composition. Claim 19 requires the ratio of fenofibrate to binding cellulose derivative is between 5/1 and 15/1.

water." It does not make any sense for some of an ingredient in the formulation to count as a percentage of the formulation, while some of the same ingredient does not. Plaintiffs are simply trying to exclude a portion of Defendants' non-infringing products to try to establish infringement.

First, the specification consistently refers to all of the binding cellulose derivative in the composition. The specification uses the phrase "binding cellulose derivative" to refer to a cellulose derivative that may be used as both a binder and a solubilization agent:

> [I]t has been discovered that the incorporation of a cellulose derivative, *used as a binder and solubilization adjuvant*, into a composition containing micronized fenofibrate and a surfactant[,] makes it possible to obtain a bioavailability which is greater than for a composition containing a comicronizate of fenofibrate and of a surfactant.

Ex. 1, '574 pat., col. 2, ll. 4–10 (emphasis added). The specification consistently explains that the invention includes a cellulose derivative that is capable of acting as a binder and a solubilization adjuvant/agent, and that HPMC is preferred. For example, the specification states that, "[a] subject of the present invention is therefore a pharmaceutical composition containing micronized fenofibrate, a surfactant *and a binding cellulose derivative, which is a solubilization adjuvant, preferably hydroxypropylmethylcellulose* (HPMC)." *Id.* ll. 11–15 (emphasis added).

The specification never limits the meaning of "binding cellulose derivative" to only a portion of the amount in the formulation, and never disregards any portion when calculating the claimed weight percents or ratio. Each of the examples provided in the specification calculates the weight percent of cellulose derivative in the composition by considering ***all*** of the cellulose derivative in the formulation. *See id.* Example 1A (weight (mass) percentage of binding cellulose derivative (HPMC) reflects the total amount of cellulose derivative); Example 1B

(same); Example 1C (same); Example 2B (same). Nor does the patent describe any way of determining whether different portions of an ingredient are performing different functions.

Second, the prosecution history further confirms that the phrase "binding cellulose derivative as a solubilization adjuvant/agent" refers to the total amount of the cellulose derivative in the composition. During prosecution, the Examiner repeatedly rejected the claims of the '574 patent as an obvious variation of the composition disclosed in Stamm, *i.e.*, the '670 patent. Ethypharm acknowledged that Stamm disclosed a composition that contained the same *ingredients* as claimed in the '574 patent—a composition comprising an inert carrier, micronized fenofibrate, a hydrophilic polymer[12] (such as HPMC), and a surfactant. *See* Ex. 21 at 12–13. The compositions disclosed in Stamm contained 5-50% by weight fenofibrate and between 20–60% hydrophilic polymer. Ex. 4, '670 pat., col. 5, ll. 3–5.

Ethypharm argued that the narrow claims of the '574 patent were, nonetheless, patentable over Stamm because they were limited to different weight percentages and ratios of the ingredients. For example, Ethypharm stated that, "Stamm unequivocally teaches that the hydrophilic polymer *must be at least 20%* by weight. Applicants claim that the corresponding element must be between 2 – 15% by weight." Ex. 21 at 13. Ethypharm repeatedly and consistently argued that the claims were patentable because Stamm disclosed compositions containing greater percentages of HPMC than were claimed in the '574 Patent. *Id.* ("Stamm does not encompass, nor does it abut, the claimed ranges."); Ex. 24 at 14 (in Stamm, "one must

[12] Stamm's hydrophilic polymer corresponds to the "binding cellulose derivative as a solubilization adjuvant/agent" in the '574 patent. *See* Ex. 19 at 12–13 (stating that Stamm discloses a composition in which "the hydrophilic polymer solubilizing agent is *at least 20%* by weight of the composition"); *id.* at 14 (stating that the hydrophilic polymer of Stamm "enhances dissolution of the fenofibrate").

use at least 20% by weight hydrophilic polymer by weight of the composition" whereas "Applicants' claimed granules contain 2 – 15% by weight of binder").

In eventually allowing the claims of the '574 patent, the Examiner similarly stated that the claims require "specific percentages of micronized fenofibrate and cellulose binder or their ratios" and that, "the prior art of record does not teach the claimed percentages (or ratios) of fenofibrate and the binder." Ex. 29 at 3.

Stamm never disregards any portion of the hydrophilic polymer in calculating its weight percent. Ethypharm never disregarded any portion of the ingredients in Stamm in distinguishing those compositions during prosecution. Nor did Ethypharm ever attempt to ascertain whether any portion of the cellulose derivative in Stamm performed any particular function. On the contrary, Ethypharm repeatedly distinguished and criticized Stamm based purely on the total amount and percent of cellulose derivative in the Stamm formulation. *See* Ex. 24 at 12 ("Unlike the '670 patent [Stamm] formulations, however, the pharmaceutical formulations of the present invention increase the percentage of fenofibrate, and decrease the percentage of binder."); *Id.* ("The claimed pharmaceutical compositions constitute more fenofibrate relative to binder than the compositions of the '670 patent[.]"); *see* Ex. 19 at 15 (Mar. 18, 2005) ("The composition [of the '574 patent] overcomes deficiencies of Stamm's compositions by using less binder").

Distinguishing Stamm on the basis of a high amount and percentage of binder would have been meaningless if the portion above a certain amount or percent could be disregarded. Accordingly, the comparisons to, and criticisms of, the ranges disclosed in Stamm reflect Ethypharm's and the Examiner's understanding that the weight percentages claimed in the '574 Patent are calculated based on the total amount of the ingredient in the formulation.

Nowhere in the patents or the prosecution histories do the Applicants refer to "binding cellulose derivative" as anything less than all of the binder in the composition. There is no support for any construction that would disregard a portion of the binding cellulose derivative. Accordingly, Defendants' proposed construction should be adopted because it clarifies that "any and all" HPMC (or other appropriate polymer) in the composition is considered.

Third, the cellulose-based polymers must also be water soluble. During prosecution, the Applicants clarified that the binder/solubilization adjuvant must be water-soluble. In distinguishing a reference that contained a polymer that was not water-soluble, the Applicants unequivocally stated: "Cross-linked polyvinylpyrrolidone *is not water soluble, which is a requirement of the solubilization adjuvant (binder) of the present invention*." Ex. 24 at 10 (emphasis added). This statement confirms that the Applicants used the phrases "binder" and "solubilization adjuvant" interchangeably to refer to the same ingredient in the claimed formulation. It also confirms that being water-soluble "is a requirement" of the claimed cellulose derivative that should be included in the construction.

9. The Calculation Limitations

"wherein said fenofibrate is present in an amount greater than or equal to 60% by weight, relative to the weight of said pharmaceutical composition"

Plaintiffs' Construction	Defendants' Construction
weight of said micronized fenofibrate in said pharmaceutical composition divided by the weight of said pharmaceutical composition times 100 must be greater than or equal to 60	weight of all of the micronized fenofibrate in the pharmaceutical composition divided by the weight of the pharmaceutical composition times 100 must be greater than or equal to 60

"wherein said binding cellulose derivative represents between 2 to 15% by weight, relative to the weight of said pharmaceutical composition"

Plaintiffs' Construction	Defendants' Construction
weight of said binding cellulose derivative as a solubilization adjuvant/agent in said pharmaceutical composition divided by the weight of said pharmaceutical composition times 100 is between 2 to 15	weight of all of the binding cellulose derivative in the pharmaceutical composition divided by the weight of the pharmaceutical composition times 100 is between 2 to 15

"said hydroxypropylmethylcellulose represents between 5 and 12% by weight of the composition" (applies to the '331 patent)

Plaintiffs' Construction	Defendants' Construction
weight of said hydroxypropylmethylcellulose in the composition divided by the weight of the composition times 100 is between 5 to 12	weight of all of the hydroxypropylmethylcellulose in the pharmaceutical composition divided by the weight of the pharmaceutical composition times 100 is between 5 and 12

"wherein the mass ratio of said fenofibrate to said binding cellulose derivative is between 5/1 and 15/1"

Plaintiffs' Construction	Defendants' Construction
weight of said micronized fenofibrate in said pharmaceutical composition divided by the weight of binding cellulose derivative as a solubilization adjuvant/agent is between 5 and 15	weight of all of the micronized fenofibrate divided by the weight of all of the binding cellulose derivative is between 5 and 15

"wherein the mass ratio of said fenofibrate to said hydroxypropylmethylcellulose is between 5/1 and 15/1" (applies to the '331 patent)

Plaintiffs' Construction	Defendants' Construction
weight of said micronized fenofibrate in the composition divided by the weight of said hydroxypropylmethylcellulose in the composition is between 5 and 15	weight of all of the micronized fenofibrate divided by the weight of all of the hydroxypropylmethylcellulose is between 5 and 15

The three independent claims of the patents-in-suit contain five calculation limitations. These five limitations refer to: (a) the weight percentage of micronized fenofibrate or binding cellulose derivative in the pharmaceutical composition; or (b) the ratio of micronized fenofibrate to binding cellulose derivative. The parties agree on the mathematical method for calculating the

percentage. But, as discussed above, they disagree on whether some portion of the micronized fenofibrate or binding cellulose derivative in the composition may be disregarded to try to show infringement. Defendants' constructions make it clear that the calculations must include "all of" the micronized fenofibrate, binding cellulose derivative or HPMC in the pharmaceutical composition, as the case may be. For all the reasons discussed above with respect to the binding cellulose derivative, the weight percentages and ratios in the pharmaceutical composition must be based on the total amount of the ingredient (micronized fenofibrate, binding cellulose derivative, or HPMC) in the pharmaceutical composition. There is simply no support in the patent specifications or the prosecution histories for disregarding any portion when performing these calculations.

On the contrary, during prosecution, Ethypharm expressly calculated the weight percent of the compositions of the prior art based on *all* fenofibrate and cellulose polymer in the formulation. For example, Ethypharm specifically relied on Example 1 of Stamm to argue during prosecution that Stamm's composition was outside the claims of the '574 patent. Ethypharm expressly stated that, "Example 1 of Stamm prepares granules containing 31.6% PVP and 31.6% micronized fenofibrate." Ex. 18 at 12. This means that Ethypharm calculated the weight percent of both the micronized fenofibrate and the cellulose derivative by dividing the total weight of each ingredient in the formulation (100 g for the micronized fenofibrate and 100 g for the binding cellulose derivative) by the total combined weight of the formulation (316.3 g). *See* Ex. 4, '670 pat., col. 6, l. 62–col. 7, l. 12 (disclosing that Stamm's Example 1 contains 2.0 g of surfactant (sodium laurylsulfate), 100 g of micronized fenofibrate, and 100 g of hydrophilic polymer (non-cross-linked PVP) on 114.3 g of inert carrier (lactose), which means the total weight of the resulting granule is 316.3 g). Plaintiffs never suggested that only a portion of the

fenofibrate or the cellulose polymer should be considered when calculating the weight percentages. *Id.*

Also, as discussed above, Ethypharm calculated the weight percent of micronized fenofibrate in the prior art 200 mg TRICOR® capsules during prosecution by dividing the total amount of micronized fenofibrate by the total weight of the contents of the capsules. Ex. 25 at 2, ¶ 7. It further calculated the weight percent for the prior art 160 mg TRICOR® tablets the same way, namely by dividing the total amount of micronized fenofibrate by the total weight of the tablets. *Id.* at ¶ 9. Ethypharm never suggested that the calculations should, or even could, be based on a functional-based subset of the fenofibrate. They simply divided the weight of fenofibrate by the weight of the pharmaceutical composition.

These calculations confirm that Ethypharm understood and represented that the method for calculating the weight percent for purposes of the '574 patent was to consider *all* (*i.e.*, the entire amount) of the ingredient in the formulation, based on the written formulation where known, and otherwise based on empirically determined average amounts. Plaintiffs cannot assert that the calculations should be performed one way during prosecution to avoid the prior art, and a different way during litigation to try to ensnare non-infringing products. There can be no dispute that the weight percent calculations in the '574 and '331 patents consider "all of" the micronized fenofibrate or binding cellulose derivative, respectively, divided by the total weight of all of the active and inactive ingredients in the final dosage form.

Finally, both patents-in-suit also contain limitations that the mass ratio of the fenofibrate to the binding cellulose derivative (or HPMC) is between 5/1 and 15/1. For the reasons previously discussed, this calculation is also based on "all of" (i.e., the total amount of)

micronized fenofibrate and the total amount of binder (or HPMC) in the composition, as reflected in Defendants' proposed construction.

The '331 Patent

10. "hydroxypropylmethylcellulose"

Plaintiffs' Construction	Defendants' Construction
a cellulose hydroxypropylmethyl ether that acts to bind the micronized fenofibrate to the neutral core and increases the micronized fenofibrate's solubility and/or rate of solubilization	the total of any and all grades of HPMC in the pharmaceutical composition

Claim 1 of the '331 patent expressly claims a preferred type of cellulose derivative—hydroxypropylmethylcellulose, or HPMC for short. The dispute regarding the meaning of this term parallels the dispute regarding the meaning of the "binding cellulose derivative as a solubilization adjuvant/agent" described above. Specifically, the dispute is whether the term refers to *all* of the HPMC in the pharmaceutical composition (Defendants' position), or only a portion thereof (Plaintiffs' position).

As set forth above, in both the patent specifications and the prosecution histories, Ethypharm consistently calculated the weight percentages of the HPMC in the prior art formulations, particularly Stamm, and in the claimed invention, based on all of the HPMC in the pharmaceutical formulation. Ethypharm then relied on this method of calculation to distinguish the prior art and argue for patentability. Accordingly, for the same reasons set forth above, the Court should construe the term as meaning, "the total of any and all grades of HPMC in the pharmaceutical composition."

Moreover, claim 1 of the '331 patent does not contain any language describing or limiting the type of HPMC to be used. Claim 1 simply recites HPMC, and requires that "said" HPMC be present in certain ratios and percentages. Plaintiffs' argument that even this

straightforward language should somehow allow them to disregard a portion of the HPMC in the formulation to try to show infringement reveals Plaintiffs' arguments for what they are—a legally impermissible attempt to avoid the narrow percentage and ratio limitations that were the basis for patentability. The Court should reject Plaintiffs' arguments and confirm that the claims have the same meaning during litigation as they did during prosecution. The claims are limited to formulations containing the claimed ratios and percentages based on all of the ingredients in the formulation.

11. "sugar"

Plaintiffs' Construction	Defendants' Construction
lactose, mannitol, sucrose or other pharmaceutically acceptable monosaccharide or other lower oligosaccharide	lactose, mannitol, sucrose or other pharmaceutically acceptable monosaccharide or other lower oligosaccharide; not a starch or other polysaccharide

Claim 1 of the '331 Patent requires a specific type of core that, "comprises a sugar or a sugar mixed with starch." The limitation draws a distinction between a "sugar" on the one hand and a "starch" on the other. It requires that the core contains either a sugar, or a mixture of a sugar and a starch. This limitation does *not* cover a core that contains starch without any sugar.

The parties' proposed constructions of the term "sugar" differ only in that Defendants' definition describes the distinction between a "sugar" and a "starch." Sugars and starches are both made up of "saccharides." They differ in the number of saccharide units. The parties appear to agree that a "sugar" includes monosaccharides (which contain one saccharide unit), lower oligosaccharides (which contain a very small number of saccharide units), and specifically includes the sugars mentioned in the '331 patent. In contrast, a "starch" is a polysaccharide (which contains many saccharide units). *See* Ex. 16, Handbook of Pharmaceutical Excipients 725 (5th ed. 2006). Accordingly, the Court should construe the term sugar as meaning, "lactose,

mannitol, sucrose or other pharmaceutically acceptable monosaccharide or other lower oligosaccharide; not a starch or other polysaccharide."

Plaintiffs' objection to the last portion of this definition, which distinguishes a starch from a sugar, suggests that Plaintiff may try to argue that a core containing only starch could still infringe because a starch is somehow a sugar. Defendants request that the Court construe the term "sugar" to preclude any such arguments.

CONCLUSION

For the reasons set forth above, Defendants ask the Court to adopt their constructions of the disputed claim terms.

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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

LUPIN ATLANTIS HOLDINGS S.A. and ETHYPHARM S.A., Plaintiffs,	:	ECF Case
	:	Case No. 1:11-cv-00668 (JSR)
v.	:	
PADDOCK LABORATORIES, INC. and CEROVENE, INC., Defendants.	:	**CERTIFICATE OF SERVICE**

I, Joel M. Wallace, hereby certify that on the 21st day of June, 2011, I caused a true and correct copy of Defendants' Opening Claim Construction Brief to be served via the Court's CM/ECF system:

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